Fate of paclitaxel lipid nanocapsules in intestinal mucus in view of their oral delivery

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Résumé en anglais

The bioavailability of paclitaxel (Ptx) has previously been improved via its encapsulation in lipid nanocapsules (LNCs). In this work, the interactions between LNCs and intestinal mucus are studied because they are viewed as an important barrier to successful oral delivery. The rheological properties of different batches of pig intestinal mucus were studied under different conditions (the effect of hydration and the presence of LNCs). Fluorescence resonance energy transfer (FRET) was used to study the stability of LNCs in mucus at 37°C for at least 3 hours. Diffusion through 223, 446, and 893 µm mucus layers of 8.4, 16.8, and 42 µg/mL Ptx formulated as Taxol® (Bristol-Myers Squibb, Rueil-Malmaison, France) or encapsulated in LNCs (Ptx-LNCs) were investigated. The effect of the size of the LNCs on their diffusion was also investigated (range, 25–110 nm in diameter). Mucus behaves as a non-Newtonian gel with rheofluidifying properties and a flow threshold. The viscous (G″) and elastic (G′) moduli and flow threshold of the two mucus batches varied with water content, but G′ remained below G″. LNCs had no effect on mucus viscosity and flow threshold. The FRET efficiency remained at 78% after 3 hours. Because the destruction of the LNCs would lead to a FRET efficiency below 25%, these results suggest only a slight modification of LNCs after their contact with mucus. The diffusion of Taxol® and Ptx-LNCs in mucus decreases if the mucus layer is thicker. Interestingly, the apparent permeability across mucus is higher for Ptx-LNCs than for Taxol® for drug concentrations of 16.8 and 42 µg/mL Ptx ($P<0.05$). The diffusion of Ptx-LNCs through mucus is not size-dependent. This study shows that LNCs are stable in mucus, do not change mucus rheological properties, and improve Ptx diffusion at low concentrations, thus making these systems good candidates for Ptx oral delivery. The study of the physicochemical interaction between the LNC surface and its diffusion in mucus is now envisioned.

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